

## Acute rheumatic fever: Presentation with early arthritis in adults

Acute rheumatic fever in adults

İsmail Doğan<sup>1</sup>, Osman Nuri Koyun<sup>2</sup>, Hakan Apaydın<sup>3</sup><sup>1</sup> Department of Rheumatology and Internal Medicine, Medicine Faculty, Ankara Yıldırım Beyazıt University, Ankara<sup>2</sup> Department of Internal Medicine, Medicine Faculty, Hitit University, Çorum<sup>3</sup> Rheumatology Clinic, Ankara City Hospital, Ankara, Turkey**Abstract**

**Aim:** Acute rheumatic fever (ARF) is a common disease in Turkey, most common between the ages of 6 and 20 years. It is rare in adults, and its clinical course differs from that in children. The aim of the study was to determine the clinical course of ARF in adults.

**Material and Methods:** Five patients who were admitted to our rheumatology outpatient clinic in a tertiary medical center located in Çorum province, with early-onset arthritis between 2017 and 2020 were diagnosed with ARF-associated arthritis. Acute rheumatic fever-associated arthritis was diagnosed according to Jones's criteria.

**Results:** The age of the cases was between 35 and 56 (mean age 45.6 years), two of them were men and three were women. One patient had atrial fibrillation and one had coronary artery disease as comorbidities. Arthritis developed in all patients after a history of tonsillitis in the last 15-21 days, and morphological changes suggesting valve involvement were detected in the echocardiogram. Two of the patients had a previous history of ARF.

**Discussion:** Acute rheumatic fever should be considered in the differential diagnosis of arthritis that develops after an upper respiratory tract infection in adults with post-streptococcal reactive arthritis.

**Keywords**

Acute Rheumatic Fever, Arthritis, Carditis

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Corresponding Author: İsmail Doğan, Rheumatology Clinic, Ankara City Hospital, Bilkent, Çankaya, Ankara, Turkey.

E-mail: dridogan@hotmail.com P: +90 505 477 01 36

Corresponding Author ORCID ID: <https://orcid.org/0000-0002-7603-9484>

Introduction

Acute rheumatic fever (ARF) is an inflammatory reaction that presents with joint, cardiac, neurological and dermatological symptoms 2-3 weeks after group A beta-hemolytic streptococcal infection. It is most commonly seen between the ages of 5-14 years. Its incidence is reported to be 0.5-3: 100.000 in developed countries and 20-100: 100.000 in developing countries [1]. Turkey is among the countries with a medium-high risk for developing ARF [2]. Since the advent of antibiotics, the incidence of rheumatic heart disease (RHD) has been low in developed countries [3,4]. However, clinically inapparent streptococcal infections or symptomatic patients not seeking care are common reasons of delayed diagnosis of ARF in developed countries [3]. This delay in diagnosis and proper management is notorious for leading to the development of RHD, which is caused by autoimmune damage of cardiac tissue and can result in severe valvular damage requiring valvular surgery [5]. Early diagnosis and management of ARF is crucial since the risk of valvular damage can be reduced with proper treatment [3]. ARF is a rare condition in adults therefore, while juvenile ARF may be overdiagnosed, the diagnosis may be overlooked in adults with rheumatic symptoms whose cardiac state inexplicably deteriorates [6]. In one of the most recent studies, it was reported that the clinical manifestations of ARF in adults were similar to that seen with ARF in children, with migratory polyarthritis being the most common manifestation [7]. In 2015, the Jones criteria were revised with the addition of monoarthritis and polyarthralgia to migratory polyarthritis and subclinical carditis findings in echocardiography as major criteria in medium-high risk populations [8]. In this study, we present case series of adult ARF, presenting with arthritis.

Material and Methods

The study was approved by the Ethics Committee (No. E1-20-324). Five adult patients who were admitted to our rheumatology outpatient clinic with early-onset arthritis between 2017-2020 and who were diagnosed with ARF-related arthritis according to Jones criteria [8] were included in this report. Hospital records of the cases were retrospectively reviewed. Arthritis, carditis, Sydenham chorea, erythema marginatum, subcutaneous nodule, fever, arthralgia, echocardiography, electrocardiogram findings, anti-streptolysin O antibody titer follow-up, erythrocyte sedimentation rate, comorbid diseases,

applied medications and treatment responses were recorded. Statistical analysis was performed using the Statistical Package for Social Science (SPSS) software, version 15.0 statistical package program (IBM Inc.; Chicago, IL, USA). Demographic and clinical variables were summarized as proportions.

Results

The ages of the patients ranged from 35 to 56 years (mean age 45.6 years), two males and three females. One patient had coronary artery disease, and one patient had atrial fibrillation as comorbidity. All of them had a history of tonsillitis 15-21 days ago. Two patients had a previous anamnesis of ARF. Clinical and laboratory findings of the cases are given in Table-1. The patients were diagnosed with acute rheumatic fever-related arthritis with a gradual increase of ASO titer within 2 weeks, migratory polyarthritis, carditis findings with echocardiography, fever and high sedimentation rate according to revised Jones criteria. For differential diagnosis of early arthritis, antinuclear antibody, anti-CCP, rheumatoid factor, uric acid and Brucella agglutination serum levels of patients were found to be negative. As a treatment, non-steroidal anti-inflammatory drugs, oral methyl prednisolone (16 mg/day) and benzathine penicillin G (1.2 million units/4 weeks-intramuscular) were prescribed. The methylprednisolone dose was gradually decreased and discontinued according to the clinical follow-up in medium 4-6 weeks. In one patient who was using warfarin for atrial fibrillation, intramuscular depo-penicillin was not given due to the risk of hemorrhage. In another patient with coronary artery disease with a planned coronary by-pass operation, methyl prednisolone was given at a dose of 4mg/day. Arthritis symptoms in all patients improved with treatment. Regular cardiology follow-ups for carditis were recommended.

Discussion

In our cases, arthritis and carditis were the major signs of ARF. Other major findings such as chorea, subcutaneous nodule and erythema marginatum were absent. Echocardiographic findings of carditis were detected in all cases. Our findings were similar to the ARF case series published in 1980, in which arthritis and carditis were among the only defined major criteria for adults [6]. In a study of 35 cases, all but one patient had migratory

Table 1. Clinical and laboratory findings of the cases

Case	Age/ Gender	Previous history suggestive of ARF	Echocardiography findings	Arthritis	Sydenham chorea/ subcutaneous nodule/erythema marginatum	Minor criteria: arthralgia	Anti-streptolysin -O antibody	Anti-streptolysin -O antibody
						Fever		
						ESR	(0-200 IU/ml) (initial application)	(0-200 IU/ml) (2 weeks later)
						PR interval elongation		
1	35/F	absent	2° MR	polyarthritis	-	+	250	430
2	42/M	present	mild MS	polyarthritis	-	+	332	472
3	42/F	absent	1-2° AR	polyarthritis	-	+	386	500
4	53/F	absent	Mild MD 2° AR 2° TR	polyarthritis	-	+	260	320
5	56/M	present	1° AR	polyarthritis	-	+	364	456

ESR: Erythrocyte Sedimentation Rate, AR:Aortic regurgitation, MR:Mitral regurgitation, MS:Mitral stenosis, TR:Tricuspit regurgitation

polyarthritis, none had chorea, erythema marginatum, or subcutaneous nodules. Carditis occurred in eight, manifested by pericarditis in four and new significant murmurs developed in four [9]. In an adult ARF series of 31 cases, arthritis was the most common major criterion. However, unlike other series, cardiac involvement was a prominent feature [10]. In a case series of 14 adult patients with ARF, all had arthritis, 4 patients had carditis. One patient had erythema marginatum, while chorea and subcutaneous nodules were not seen. Of these, only 3 had a childhood history of rheumatic fever [11]. On the other hand, two patients had a childhood history of rheumatic fever in our study.

ARF in adults was studied on the basis of an analysis of 23 patients, together with a review of a further 466 published cases [6]. In contrast to juvenile ARF, in this study, only arthritis (83%) and carditis (35%) were major criteria for the diagnosis in an analysis of 23 patients [6]. In a series of 25 ARF patients, the incidence of prolonged PR-interval was found to be higher with adult-onset disease [12]. Likewise, all patients had prolonged PR-interval in our study. ARF is more common in adults than previously recognized. Therefore, clinicians should be aware of this condition and include it in their differential diagnosis of febrile patients with arthritis [12].

Post-streptococcal reactive arthritis (PSRA) should be considered in the differential diagnosis of ARF. Sahin et al. reported a series of 43 cases in adults (6 ARF, 37 PSRA). In the PSRA group, unlike the ARF group, mono-oligo arthritis was more frequent than migrating arthritis. No signs of fever and carditis were detected in any of the cases [13]. In our study, there was migrating arthritis and fever in ARF cases, and all of them had signs of carditis in echocardiography.

ARF is no longer a public health problem in developed countries with high socioeconomic status. But its prevalence in school-age children >2/100,000, all age>1/1000th of the developing countries, including Turkey; take part in middle-high risk countries [2].

The incidence of ARF is high in children aged 5-14 years. ARF is not usually seen in children under 5 years of age. It is rare to be seen as the first episode in adults over 30 years of age, and the risk of recurrence decreases in adults over 40 years of age. Although there is no significant gender discrepancy, heart involvement is reported to be more common in females [5]. In our report, ARF was detected as the first episode in patients over 30 years of age for 3 cases. Recurrence was observed in 2 cases over 40 years old with an anamnesis of ARF.

The diagnosis of ARF is often more difficult for several reasons because of similarities to other polyarthritis common in adults, such as early rheumatoid arthritis, systemic lupus erythematosus, gout and the like, and major symptoms such as Sydenham chorea, erythema marginatum and carditis are less common in adults. In addition, in a patient with previous rheumatic heart disease, the presence of heart murmurs, as well as of various non-specific findings such as fever, increased acute phase reactants and electrocardiographic abnormalities may demonstrate complications of rheumatic heart disease other than recrudescence of activity.

Our rheumatology clinic is the only rheumatology clinic in Çorum province with a population of 500,000, and the fact that only 5

cases were detected in adult patients presenting with arthritis in 2 years may suggest that ARF is not frequently presented with arthritis in adults in that region. However, further studies of the incidence of ARF cases presenting with carditis to cardiology and chorea to neurology clinics in adulthood may be indicative of the incidence of ARF in adulthood.

Acute rheumatic fever-related arthritis is not a common condition in adult patients and should be kept in mind for patients with arthritis after upper respiratory tract infections since early recognition may prevent heart complications.

#### Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

#### Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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#### Conflict of interest

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